
Guidance for Industry

Information Program on Clinical Trials for Serious or Life-Threatening Diseases: Establishment of a Data Bank

DRAFT GUIDANCE

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**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
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GUIDANCE FOR INDUSTRY¹

I. INTRODUCTION

This guidance is intended to provide recommendations for sponsors of investigational new drug applications (INDs) on submitting information about clinical trials for serious or life-threatening diseases to a Clinical Trials Data Bank. Section 113 of the Food and Drug Administration Modernization Act (Modernization Act) required the establishment of this data bank and specified what information was to be submitted for it.

This guidance document addresses only the statutory requirements for submission of protocol information to the Clinical Trials Data Bank. An implementation plan, addressing procedural issues, will be available later in 2000. The implementation plan will include information such as how to submit protocols to the Clinical Trials Data Bank and how to provide certification to the Secretary that disclosure of information for a particular protocol would substantially interfere with the timely enrollment of subjects in the clinical investigation.

Until the implementation plan is available, sponsors submitting clinical trials information for inclusion in the AIDS Clinical Trials Information Service (ACTIS) data bank should continue to follow procedures currently in place. Non-NIH sponsors of clinical trials for other serious or life-threatening diseases need not provide clinical trials information for the data bank until after procedures are described in the implementation plan that will be available later this year. When the procedures are issued, we will establish a time frame for submitting information.

II. BACKGROUND

Section 113 of the Modernization Act provides for the public availability of specified information on studies of drugs for serious or life-threatening diseases conducted under FDA's IND regulations (21 CFR part 312).

¹ This guidance has been prepared by the Implementation Team for FDAMA Section 113, including individuals from the Office of the Commissioner, the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Center for Devices and Radiological Health (CDRH), at the Food and Drug Administration. This guidance document represents the Agency's current thinking on the information program on clinical trials for serious or life-threatening diseases. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes, regulations, or both.

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The Modernization Act, enacted November 21, 1997, amends section 402 of the Public Health Service Act (42 U.S.C. 282) and directs the Secretary of Health and Human Services, acting through the Director, National Institutes of Health (NIH), to establish, maintain, and operate a data bank of information on clinical trials of new treatments for serious or life-threatening diseases and conditions. Activities related to the Clinical Trials Data Bank are to be coordinated and integrated among the agencies in the Department of Health and Human Services (DHHS) and, to the extent practicable, with other data banks containing similar information.

The Clinical Trials Data Bank is intended to be a central resource providing current information on clinical trials to individuals with serious or life-threatening diseases, to other members of the public, and to healthcare providers and researchers. Specifically, the Clinical Trials Data Bank will contain (1) information about clinical trials, both federally and privately funded, of experimental treatments (drugs, including biological products) for patients with serious or life-threatening diseases, (2) a description of the purpose of the experimental drug, (3) patient eligibility criteria, (4) the location of clinical trial sites, and (5) a point of contact for patients wanting to enroll in the trial. Section 113 of the Modernization Act specifies that information in the Clinical Trials Data Bank must be in a form that can be readily understood by members of the public.

The National Library of Medicine (NLM) at NIH is developing the Clinical Trials Data Bank and implementing it in a phased approach. The first public version was made available on February 29, 2000. The new database can be reached at <http://clinicaltrials.gov>. It includes primarily NIH-sponsored trials in various data banks within NIH (e.g., NIH Intramural Clinical Center Studies, PDQ/National Cancer Institute) and information about federally and privately sponsored HIV/AIDS trials made available through ACTIS. Later in 2000, data from other Federal agencies and the private sector will be incorporated. This information is to be made available through various types of information systems, including a toll-free telephone number.

III. STATUTORY REQUIREMENTS FOR IND SPONSORS

A. Data Requirements

Section 113 of the Modernization Act requires that sponsors submit to the Clinical Trials Data Bank a description of the purpose of each experimental drug, patient eligibility criteria for the trial, the location of clinical trial sites, and a point of contact for those wanting to enroll in the trial. The statute requires that this information be provided in a form that can be readily understood by members of the public.

FDA and NIH developed these data elements based on the legislative requirements and comments submitted to Docket 98D-0293, *Section 113 NIH Data Bank — Clinical Trials for Serious Diseases*. These elements fall into four general areas:

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- **Descriptive Information**
 - Brief Title
 - Brief Protocol Summary
 - Study Design/Study Phase/Study Type
 - Condition or Disease
 - Intervention
- **Recruitment Information**
 - Study Status
 - Eligibility Criteria/Gender/Age
- **Location and Contact Information**
 - Location of Trial/Site
 - Contact
- **Administrative Data**
 - Study ID Number
 - Data Provider/Study Sponsor
 - Date Last Modified

B. Time Requirements

Section 113 of the Modernization Act requires that sponsors forward information to the Clinical Trials Data Bank no later than 21 days after approval. Protocols conducted under FDA's IND regulations (21 CFR part 312) require prior approval by the appropriate institutional review board (IRB). FDA does not specifically approve an IND protocol. Therefore, the Agency recognizes the need to clarify the date of submission to the data bank. For purposes of responding to this section of the Modernization Act, sponsors should submit protocol information to the Clinical Trials Data Bank (1) no later than 21 days after the trial is first opened for enrollment, (2) upon amending the protocol with respect to one of the required data elements, or (3) when recruitment for the study is interrupted, resumed, or completed.

C. Institutional Review Board Requirements

Questions have been raised about whether information listed in the Clinical Trials Data Bank would constitute ***advertising for patient recruitment***, requiring prior IRB review and approval. The 1998 update of *Information Sheets: Guidance for Institutional Review Boards and Clinical Investigators* (<http://www.fda.gov/oc/oha/IRB/toc4.html#Recruiting%20StudySubjects>) provides guidance on IRB review and approval of listings of clinical trials on the Internet. It recommends that review of listings need not occur when the system format limits the information provided to basic information, such as the title, the purpose of the study, protocol

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summary, basic eligibility criteria, study site locations, and how to contact the site for further information. The format for the Clinical Trials Data Bank is consistent with this guidance. Therefore, prior IRB approval for submitting this information to the Clinical Trials Data Bank is not required.

D. Certification Requirements

Section 113 of the Modernization Act specifies that the data bank will not include information relating to a trial if the sponsor certifies to the Secretary of DHHS that disclosure of the information would substantially interfere with the timely enrollment of subjects in the investigation, unless the Secretary makes a determination to the contrary. The Secretary will make a final determination on the sponsor's waiver request, and if the Secretary determines that such disclosure would *not* substantially interfere with enrollment, the trial is to be included in the Clinical Trials Data Bank. Submission of waiver requests will be discussed in more detail in the implementation document that will be available later in 2000.

E. Voluntary Information

Section 113 of the Modernization Act also specifies that if a sponsor consents, the Clinical Trials Data Bank can include information pertaining to results of clinical trials, including information on potential toxicities or adverse effects associated with the use or administration of the investigational treatment. Sponsors may also voluntarily include studies that are not trials to test effectiveness or not for serious or life-threatening diseases in the Clinical Trials Data Bank. Inclusion of voluntary information in the Clinical Trials Data Bank will be addressed in more detail in the implementation document to be available later in 2000.

IV. IDENTIFICATION OF TRIALS FOR A SERIOUS OR LIFE-THREATENING DISEASE

The Modernization Act specifies that information about clinical trials for serious or life-threatening diseases be made publicly available through a clinical trials data bank. In 1988, FDA issued interim regulations on Drugs Intended to Treat Life-Threatening and Severely-Debilitating Illnesses (21 CFR 312 subpart E). Subpart E established procedures to expedite the development and availability of new therapies intended to treat persons with life-threatening and severely debilitating diseases. Life-threatening was defined as: (1) diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted; and (2) diseases or conditions with potentially fatal outcomes, where the endpoint of clinical trial analysis is survival.

FDA has previously discussed serious diseases in the preamble to the final rule on Investigational New Drug, Antibiotic, and Biological Product Regulations: Treatment Use and Sale (52 FR 19466, May 22, 1987) and in the preamble to the proposed rule for the accelerated approval regulations (57 FR 13234, April 15, 1992). More recently, FDA discussed issues related to products intended to treat serious or

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life-threatening diseases in the guidance for industry on *Fast Track Drug Development Programs — Designation, Development, and Application Review* (November 1998). The seriousness of a disease is a matter of judgment, but generally is based on such factors as survival, day-to-day functioning, and the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. Acquired immunodeficiency syndrome (AIDS), all other stages of human immunodeficiency virus (HIV) infection, Alzheimer's disease, angina pectoris, heart failure, cancer, and many other diseases are clearly serious in their full manifestations. Further, many chronic illnesses that are generally well managed by available therapy can have serious outcomes. For example, inflammatory bowel disease, asthma, rheumatoid arthritis, diabetes mellitus, systemic lupus erythematosus, depression, psychoses, and many other diseases can be serious for certain populations or in some or all of their phases.

For purposes of responding to section 113 of the Modernization Act, sponsors should refer to the information about serious or life-threatening diseases provided in the guidance for industry on *Fast Track Drug Development Programs — Designation, Development, and Application Review* (<http://www.fda.gov/cder/guidance/index.htm>).

V. IDENTIFICATION OF TRIALS TO TEST EFFECTIVENESS

Section 113 of the Modernization Act specifies that the Clinical Trials Data Bank contain information about clinical trials for serious or life-threatening diseases and conditions either with the consent of a sponsor or when a trial to test effectiveness begins. Not all trials carried out under 21 CFR part 312 are trials to test effectiveness. For purposes of responding to this requirement of the Modernization Act, phase 2, phase 3, and phase 4 trials with efficacy endpoints are considered trials to test effectiveness.

Listing a trial in the Clinical Trials Data Bank is not a guarantee that the trial design is considered adequate to support approval of a drug, nor does it reflect any judgment on the adequacy of the conduct, analysis, or outcome of the study.

VI. IDENTIFICATION OF TRIALS REQUIRED TO BE INCLUDED IN THE CLINICAL TRIALS DATA BANK

Sponsors should determine which protocols meet the criteria for inclusion in the Clinical Trials Data Bank using the recommendations in this guidance on identifying trials to test effectiveness and trials for serious or life-threatening diseases. Examples of such trials are clinical trials to test effectiveness for products that receive fast track designation,² and phase 2, 3, and 4 trials with efficacy endpoints. Section 113 of the Modernization Act states that information on all treatment IND protocols and all

² See the guidance for industry on *Fast Track Drug Development Programs — Designation, Development, and Application Review* (November 1998).

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group C protocols must be included in the Clinical Trials Data Bank. Although not specifically discussed in section 113 of the Modernization Act, there are situations in which there may be a significant number of patients with the disease or condition for which the drug is being developed who are not adequately treated by existing therapy, do not meet the eligibility criteria for enrollment, or are otherwise unable to participate in a controlled clinical study. In such cases, sponsors should consider including in the Clinical Trials Data Bank information about the availability of an expanded access protocol for treatment use other than a treatment IND or group C protocol.

For protocols not specifically mentioned above, sponsors should review each protocol submitted to an IND to determine if the protocol is for a serious or life-threatening disease and if it is a trial to test effectiveness. If the protocol meets these criteria, then it should be submitted to the Clinical Trials Data Bank, unless the sponsor provides detailed certification to the Secretary that such disclosure would substantially interfere with the timely enrollment of subjects in the investigation. Sponsors with questions on whether they are required to provide information to the Clinical Trials Data Bank are encouraged to contact the appropriate review division for additional guidance.